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THE EFFECT OF SULFONYLUREAS DRUGS ON KIDNEY AND LIVER FUNCTIONS IN TYPE 2 DIABETIC PATIENTS

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Abstract

Background: Since there is an insufficiency in both insulin secretion and insulin action, so that the treatment of patients with Type 2 diabetes is more challenging than with Type 1 diabetes. In this study we estimated the effects of treatment with sulfonylureas drug in patients with Type 2 diabetes on functions of liver and kidney.
Methods: This study involved 90 individuals were divided into three groups, 30 Type 2 diabetic patients who treated with sulfonylureas drug (group 1), 30 individuals apparently healthy (group 2), as well as 30 Type 2 diabetic patients (group 3) Who diagnosed recently with Type 2 diabetes (Newly) without any treatment. Fasting serum glucose (FSG), Glycated HaemoglobinA1c (HbA1c%), liver enzymes [alanine Aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP)], blood urea (BU) , serum creatinine (SCr), and total protein (TP) levels were established. Age, disease duration, and body mass index (BMI) have all been determined. Result: Sulfonylureas had a significant impact on diabetes patients' blood sugar levels, as per the study's findings, it have a significant effect on urea levels, as well as maintain liver enzyme activity at a normal level.
Conclusion: This study confirmed that the medication with sulfonylureas had a beneficial effect in preserving the health of the liver for diabetic patients.

Keywords: Diabetes Type 2, Sulfonylureas, Iver Enzymes, Kidney Function.

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Introduction

Diabetes mellitus is a metabolic disorder caused by a deficiency with insulin secretion, action, or both. Insulin insufficiency causes chronic hyperglycemia, resulting in problems with carbohydrate, lipid, and protein metabolism (1).It's the most common endocrine condition around the worldwide , insulin secretion abnormalities are produced by insufficient insulin release due to apoptosis or insulin resistance failure in the pancreatic islets'-cells,a decrease in the efficiency of insulin-induced glucose absorption and utilization causes this condition(2).

When a body develops resistant to insulin, sugar builds up in a bloodstream, causing T2DM. When your blood sugar level is greater than normal, you have prediabetes (3). Diabetes is a chronic disease associated with many complications

. T2DM and its consequences are an important public health concern around the world, with high rates of morbidity and mortality (4). Patients with uncontrolled diabetes may have micro or macrovascular complications. In spite of

the type and duration of diabetes, these complications are widespread. Chronic hyperglycemia is linked to long-term damage and dysfunction in a variety of organ systems (5).

People with diabetes currently live longer than ever before, due to a medical advancement. Many hypoglycemic medications used in T2DM, such as sulfonylureas, metformin, thiazolidinediones, and basal insulin, provide for considerable control of fasting blood glucose .These medications are initiated as a monotherapy, such like metformin alone, and then modified to a combination treatment (metformin + sulphonylurea) if the desired glycemic control or glycated hemoglobin isn't achieved (6).

Sulfonylureas are a group of chemical compounds used in drug discovery and development, such as antidiabetic medicines that are widely used in the treatment of type 2 diabetes. They activate by causing the beta cells in the pancreas to produce more insulin (7).

Amaryl (glimepiride) is an anti-diabetic medication used to treat type 2 diabetes T2DM. It is a kind of sulfonylurea that is used in connection with a healthy diet and regular exercise to assist patients with T2DM control their blood sugar levels.T2DM. It's also possible to combine it with other diabetes drugs.Reducing high blood sugar can preventing a variety of diabetes consequences(8).

Glibenclamide (Daonil), often called as glyburide, is a T2DM medicine It is recommended that it be taken together with diet and exercise. It may be used with other antidiabetic medications (9) .Figure (1.1) demonstrates illustration of sulfonylureas and their site of action(10).

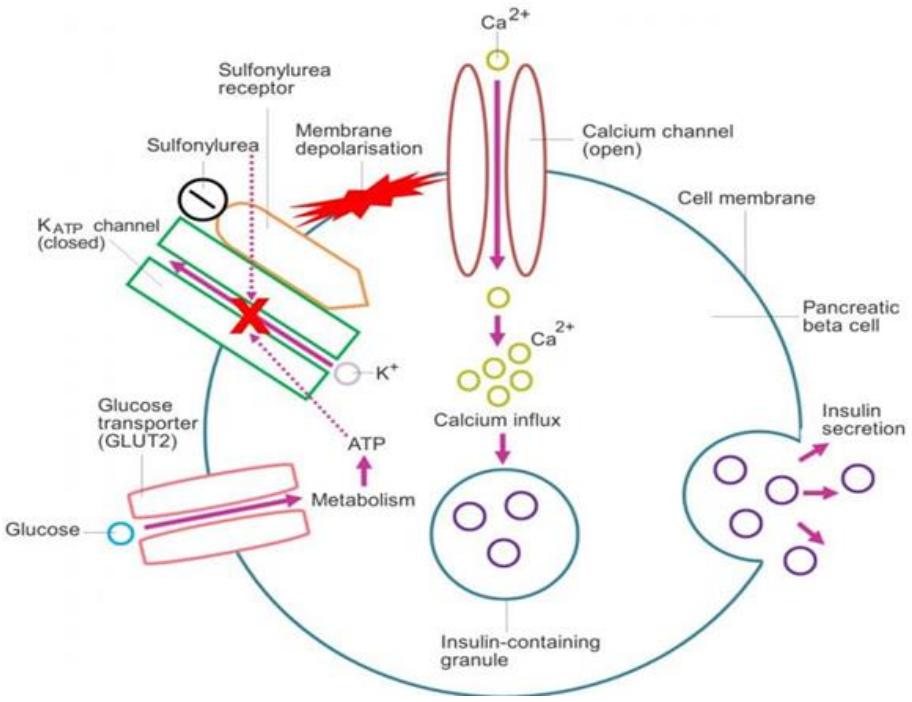

Figure1.1. Mechanism of sulfonylureas action.

Treatments for type 2 diabetes that are taken orally have unfavorable effects on the liver. Metformin is not recommended for those who have liver problems since it can cause lactic acidosis. Hepatitis marked by jaundice and itching can also be caused by chlorpropamide (11).The microvascular problem occurs in approximately 30% of people with T1DM and approximately 40% of patients with T2DM, and it is a prognostic marker in diabetic patients. (12).

Materials and Methods:

The study was conducted at Department of Applied Chemistry, College of Applied Science / University of al−Fallujah and at al-Fallujah teaching hospital . ninety individuals were enrolled in the study, and their age over 40 years,

30 of them were T2DM patients on sulfonylureas therapy (group 1), 30 were T2DM patients (newly diagnosis) without therapy (group 2), and 30 apparently healthy individual as a control group (group 3),

. A standardized questionnaire was utilized to collect detailed information about the patient's family history, age, and duration of diabetes, body mass indexwas measured for patients. Patients with other diseases ,smoking and pregnant female , patients taking other than sulfonylureas had been excluded. HbA1C% was measured using the Integrated Sciences (Australia) A1C test system, fasting serum glucose concentration was estimated by colorimetric method by using a kit supplied by Bio Systems (SPAIN), ALT kit, AST kit, and ALP kit were estimated by using a kit supplied by Agappe (Switzerland), serum urea and Creatinine were estimated by using a kit supplied by bio Systems (SPAIN) , serum total protein was estimated by using a kit supplied by Biuret method/BIOLABO SAS.

Statistical analysis

The SPSS (version 20) application was used to conduct the statistical analysis. The data was presented as mean ± SD. For the statistical test, the ANOVA test was employed to check for differences between the groups that were analyzed,the range test at p≤ 0.05 was considered significant, however the multiple range test at p≤ 0.001 was considered extremely significant, and the range test at p≥ 0.05 was considered non-significant.

Results and discussion

As previously stated, this study Involved 90 participants, which were divided into three groups. Demographic statistics (Mean SD) for all analyzed groups are shown in the table below:

Table (3-1): Levels of mean ± SD for all studied groups

parameter	G1(Treatment)	G2(Control)	G3(Newly)	P- Value
Age (year)	53.53 ± 3.24	51.13 ± 5.64	52.0 ± 5.126	Non-sig.
BMI	29.2 ± 1.52	26.4 ± 2.38	27.26 ± 2.96	Non-sig.
HbA1C (%)	8.60 ± 1.40 a	4.66 ± 0.48 a,c	7.73 ± 0.798 c	*0.05
FBS(mg/dl)	204.66 ± 50.47 a	82.60 ± 8.02 a,c	245.00 ± 34.62 c	*0.00
AST (U/L)	22.86 ± 7.09 b	20.86 ± 3.37 c	34.86 ± 6.49 b, c	*0.02
ALT (U/L)	22.53 ± 6.23 b	16.80 ± 2.75 c	32.93 ± 5.36 b,c	*0.00
ALP (U/L)	78.06 ± 16.33 b	70.26± 17.46 c	101.33 ± 15.13 b ,c	*0.05
BUN (mg/dl)	26.80± 2.17 b	25.52± 6.68 c	38.40± 1.63 b,c	*0.05
Creatinine (mg/dl)	0.7053± .177	0.6847± .123	0.7500± .100	Non-sig.
TP (g/dl)	6.7307± .649	6.6333± .515	6.7160± .869	Non-sig.

Significant using ONEWAY-ANOVA and at 0.05 level.

a, Refers to significant difference within G1 and G2

b, Refers to significant difference within G1 and G3

c, Refers to significant difference within G2 and G3

Results of this study showed no significant difference between the experimental groups, which is shown in the table above,because all patients and healthy control samples above the age of 40 were chosen, these results were obtained,There was no effect on age since samples of matching ages were chosen. Furthermore, there were no variations in BMI across the groups tested The findings of this study disagree with those of earlier studies have also shown that T2DM patients are characterized by weight increase (13).

As stated in table (3-1), the statistical levels for glycemic status (FBG and HbA1c) were conducted on all groups. FBG and HbA1c were found to be related in a study, Each of these tests are similarly efficient in diagnosing and detecting diabetes, however HbA1c is a more precise measure than FBS, It also indicates the severity of diabetes and the degree of control over it (14).The HbA1c and FBG results revealed that there are significant differences among diabetic groups (G1 and G3) and healthy control groups (G2) ($P<0.05$). A high level of HbA1c and FBG was discovered in all diabetic groups (treatment and newly diagnosed) in the current investigation, indicating poorly managed glycemia in those participants, and this finding is consistent with the findings of the following study (15).

As shown by the Table 3-1, the comparison of liver function tests (AST, ALT, ALP) between G1 and G3 is significant, implying that the treatment has a favorable effect on the liver, lowering the values of liver enzymes while maintaining their normal range .While comparing G2 and G3, there are significantly different, indicating that therapy has a beneficial effect on liver health, which is supported by the following study(16).A prior study found that ALK increases dramatically over the first two years of treatment and thereafter decreases. However, the cause is unknown at this time because no studies have been conducted to prove the source of its rise and subsequent decline. (17).

Renal function evaluation is crucial in the management of patients with renal disease or dysfunction that affects renal function. Renal function assessments might assist you in finding out if you have kidney disease (18).Table (3-1)was displayed the (mean± SD) of renal function tests performed on all study groups .There were no significant differences between the treatment and control groups in the renal function tests (urea, creatinine, and TP).The present study's findings matched those of a previous investigation (19),However, they contrasted with another study that found a relationship between elevated blood glucose levels and excessive urea and creatinine levels, as well as a reduced glomerular filtration rate(20). In this study, sulfonylureas have been shown to be effective in the treatment of type 2 diabetes patients, noting that the majority of patients who received the medication observed their urea levels have dropped to the normal range, allowing them to live better and with fewer adverse effects, indicating that the majority of patients who received the medication had seen an improvement in keeping their liver enzyme levels (AST, ALT, ALP) within the healthy range needed to keep them healthy and prevent situations.

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